Bifurcation Analysis of a Mathematical Model for Malaria Transmission *

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Abstract

We present an ordinary differential equation mathematical model for the spread of malaria in human and mosquito populations. Susceptible humans get infected at a certain probability when they contact infectious mosquitoes. They then progress through the exposed, infectious and recovered classes, before reentering the susceptible class. Susceptible mosquitoes get infected at a certain probability when they contact infectious or recovered humans and then move through the exposed and infectious classes. Both species follow a logistic model for their population growth, with humans having additional immigration and disease-induced death. For this epidemic model, we define a reproductive number, R_0 , for the number of secondary cases that one infected individual will cause through the duration of the infectious period. We find the disease-free equilibrium is locally asymptotically stable when $R_0 < 1$ and unstable when $R_0 > 1$. We prove the existence of at least one endemic equilibrium point for all $R_0 > 1$. In the absence of disease-induced death, we prove the transcritical bifurcation at $R_0 = 1$ is supercritical (forward). Numerical simulations suggest that for larger values of the disease-induced death rate, a subcritical (backward) bifurcation is possible at $R_0 = 1$.

1 Introduction

Malaria is an infectious disease caused by a parasite (Plasmodium) and transmitted between humans by the bites of mosquitoes (female Anopheles). Malaria kills about $700,\,000-2.7$ million people a year, 75% of which are African children. An estimated 40% of the world's population live in malaria endemic areas. Evidence of malaria-like diseases dates back in written history to at least

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2700 BC. The incidence of malaria has been growing due to increasing parasite drug-resistance and mosquito insecticide-resistance.

Mathematical modeling of malaria began in 1911 with Ross' model [23] and major extensions are described in MacDonald's 1957 book [18]. The first models were two-dimensional with one variable representing humans and the other representing mosquitoes. An important addition to the malaria models was the inclusion of acquired immunity proposed by Dietz, Molineaux and Thomas [9]. Further work on acquired immunity in malaria has been conducted by Aron [2] and Bailey [5]. Anderson and May [1], Aron and May [3], Koella [13] and Nedelman [19] have written some good reviews on the mathematical modeling of malaria. Some recent papers have also included environmental effects [17], [25] and [26]; the spread of resistance to drugs [4] and [14]; and the evolution of immunity [15].

Recently, Ngwa and Shu [21] and [20] proposed an ordinary differential equation (ODE) compartmental model for the spread of malaria with a Susceptible-Exposed-Infectious-Recovered-Susceptible (SEIRS) pattern for humans and a Susceptible-Exposed-Infectious (SEI) pattern for mosquitoes. In this paper, we extend and analyze this model that describes the transmission of malaria (Figure 1.1).

The model divides the human population into 4 classes: susceptible, exposed, infectious and recovered (immune). People enter the susceptible class, either through birth (at a constant per capita rate) or through migration (at a constant rate). When an infectious mosquito bites a susceptible human, there is some finite probability that the parasite (in the form of sporozoites) will be passed on to the human and the person will move to the exposed class. The parasite then travels to the liver where it develops into its next life stage. After a certain period of time, the parasite (in the form of merozoites) enters the blood stream, usually signaling the clinical onset of malaria. In our model, people from the exposed class enter the infectious class at a rate that is the reciprocal of the duration of the latent period. After some time, the infectious humans recover and move to the recovered class. The recovered humans have some immunity to the disease and do not get clinically ill, but they still harbour low levels of parasite in their blood stream and can pass the infection to mosquitoes. After some period of time, they lose their immunity and return to the susceptible class. Humans leave the population through a density-dependent per capita outward migration and natural death rate, and through a per capita disease-induced death rate.

Female mosquitoes (we do not include male mosquitoes in our model because only female mosquitoes bite animals for blood meals) enter the susceptible class through birth. The parasite (in the form of gametocytes) enters the mosquito, with some probability, when the mosquito bites an infectious human or a recovered human (the probability of transmission of infection from a recovered human is much lower than that from an infectious human); and the mosquito moves from the susceptible to the exposed class. After some period of time, dependent on the ambient temperature and humidity, the parasite develops into sporozoites and enters the mosquito's salivary glands; and the mosquito moves

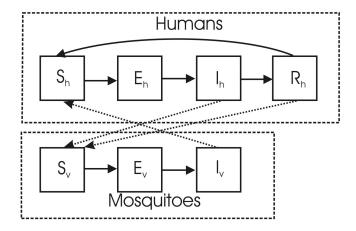


Figure 1.1: A schematic of the mathematical model for malaria transmission. Susceptible humans, S_h , get infected at a certain probability when they contact infectious mosquitoes. They then progress through the exposed, E_h , infectious, I_h , and recovered, R_h , classes, before reentering the susceptible class. Susceptible mosquitoes, S_v , get infected at a certain probability when they contact infectious or recovered humans and then move through the exposed, E_v , and infectious, I_v , classes. Both species follow a logistic model for their population growth, with humans having additional immigration and disease-induced death. Birth, death and migration into and out of the population are not shown in the figure.

from the exposed class to the infectious class. The mosquito remains infectious for life. Mosquitoes leave the population through a per capita density-dependent natural death rate.

The main differences in our model, from that of Ngwa and Shu [21], is that we have included human immigration and have excluded direct human recovery from the infectious to the susceptible class, bypassing the recovered stage. Human movement is present throughout the world and plays a large role in the epidemiology of diseases, including malaria. In many parts of the developing world, there is rapid urbanization as many people leave rural areas and migrate to cities in search of employment. We include this movement as an inward migration rate into the susceptible class. We do not include immigration of "diseased" individuals as we believe that most people who are sick will not travel. We also exclude the movement of exposed people because, given the short time of the exposed stage, the number of exposed people is small. We also exclude direct infectious-to-susceptible recovery that the model of Ngwa and Shu [21] contains. We believe that this is a valid simplifying assumption because most people show some period of immunity before becoming susceptible again. As our model includes an exponential distribution of movement from the

recovered to the susceptible class, it will include the quick return to susceptibility of some individuals. Our model is not a generalization of that of Ngwa and Shu [21]; nor is it a special case of that model.

We first describe the mathematical model including the definition of a domain where the model is mathematically and epidemiologically well-posed. Next, we prove the existence and stability of the disease-free equilibrium points, define the reproductive number and describe the existence and stability of the endemic equilibrium point(s).

2 Malaria Model

The equations for the malaria model are shown in (2.1):

$$\frac{dS_h}{dt} = \Lambda_h + \psi_h N_h + \rho_h R_h - \lambda_h S_h - f_h(N_h) S_h \qquad (2.1a)$$

$$\frac{dS_h}{dt} = \Lambda_h + \psi_h N_h + \rho_h R_h - \lambda_h S_h - f_h(N_h) S_h \qquad (2.1a)$$

$$\frac{dE_h}{dt} = \lambda_h S_h - \nu_h E_h - f_h(N_h) E_h \qquad (2.1b)$$

$$\frac{dI_h}{dt} = \nu_h E_h - \gamma_h I_h - f_h(N_h) I_h - \delta_h I_h \qquad (2.1c)$$

$$\frac{dR_h}{dt} = \gamma_h I_h - \rho_h R_h - f_h(N_h) R_h \qquad (2.1d)$$

$$\frac{dI_h}{dt} = \nu_h E_h - \gamma_h I_h - f_h(N_h) I_h - \delta_h I_h \tag{2.1c}$$

$$\frac{dR_h}{dt} = \gamma_h I_h - \rho_h R_h - f_h(N_h) R_h \tag{2.1d}$$

$$\frac{dS_v}{dt} = \psi_v N_v - \lambda_v S_v - f_v(N_v) S_v$$

$$\frac{dE_v}{dt} = \lambda_v S_v - \nu_v E_v - f_v(N_v) E_v$$

$$\frac{dI}{dI} = \lambda_v S_v - \nu_v E_v - f_v(N_v) E_v$$
(2.1e)

$$\frac{dE_v}{dt} = \lambda_v S_v - \nu_v E_v - f_v(N_v) E_v \tag{2.1f}$$

$$\frac{dI_v}{dt} = \nu_v E_v - f_v(N_v) I_v \tag{2.1g}$$

with $N_h = S_h + E_h + I_h + R_h$ and $N_v = S_v + E_v + I_v$ with

$$\frac{dN_h}{dt} = \Lambda_h + \psi_h N_h - f_h(N_h) N_h - \delta_h I_h$$
 (2.2a)

$$\frac{dN_v}{dt} = \psi_v N_v - f_v(N_v) N_v \tag{2.2b}$$

and infection rates.

$$\lambda_h = \frac{\beta_{hv}\sigma_{vh}I_v}{N_h} \tag{2.3a}$$

$$\lambda_v = \frac{\beta_{vh}\sigma_{vh}I_h}{N_h} + \frac{\tilde{\beta}_{vh}\sigma_{vh}R_h}{N_h}.$$
 (2.3b)

The state variables of the model are shown in Table 2.1 and the parameters used in the model are shown in Table 2.2. All parameters are assumed to be strictly positive with the exception of the disease-induced death rate, δ_h , which we assume to be nonnegative.

Table 2.1: The state variables for the malaria model (2.1).

- S_h : The number of susceptible humans.
- E_h : The number of exposed humans.
- I_h : The number of infectious humans.
- R_h : The number of recovered (immune and asymptomatic, but slightly infectious) humans.
- S_v : The number of susceptible mosquitoes.
- E_v : The number of exposed mosquitoes.
- I_v : The number of infectious mosquitoes.
- N_h : The total human population.
- N_v : The total mosquito population.

Table 2.2: The parameters for the malaria model (2.1).

- Λ_h : The immigration rate of humans. Dimensions: Humans \times Time⁻¹.
- ψ_h : The per capita birth rate of humans. Dimensions: Time⁻¹.
- ψ_v : The per capita birth rate of mosquitoes. Dimensions: Time⁻¹.
- σ_{vh} : The number of bites on humans per mosquito per unit time. Dimensions: Time⁻¹.
- β_{hv} : The probability of transmission of infection from an infectious mosquito to a susceptible human given that a contact between the two occurs. Dimensions: 1.
- β_{vh} : The probability of transmission of infection from an infectious human to a susceptible mosquito given that a contact between the two occurs. Dimensions: 1.
- $\hat{\beta}_{vh}$: The probability of transmission of infection from a recovered (asymptomatic carrier) human to a susceptible mosquito given that a contact between the two occurs. Dimensions: 1.
- ν_h : The per capita rate of progression of humans from the exposed state to the infectious state. $1/\nu_h$ is the average duration of the latent period. Dimensions: Time⁻¹.
- ν_v : The per capita rate of progression of mosquitoes from the exposed state to the infectious state. $1/\nu_v$ is the average duration of the latent period. Dimensions: Time⁻¹.
- γ_h : The per capita recovery rate for humans from the infectious state to the recovered state. $1/\gamma_h$ is the average duration of the infectious period. Dimensions: Time⁻¹.
- δ_h : The per capita disease-induced death rate for humans. Dimensions: Time⁻¹.
- ρ_h : The per capita rate of loss of immunity for humans. $1/\rho_h$ is the average duration of the immune period. Dimensions: Time⁻¹.
- $f_h(N_h)$: = $\mu_{1h} + \mu_{2h}N_h$. The per capita density-dependent death and emigration rate for humans. Dimensions: Time⁻¹.

 $f_v(N_v)$: = $\mu_{1v} + \mu_{2v}N_v$. The per capita density-dependent death rate for mosquitoes. Dimensions: Time⁻¹.

 μ_{1h} : The density independent part of the death (and emigration) rate for humans. Dimensions: Time⁻¹.

 μ_{2h} : The density dependent part of the death (and emigration) rate for humans. Dimensions: Humans⁻¹ × Time⁻¹.

 μ_{1v} : The density independent part of the death rate for mosquitoes. Dimensions: Time⁻¹.

 μ_{2v} : The density dependent part of the death rate for mosquitoes. Dimensions: Mosquitoes⁻¹ × Time⁻¹.

To analyze the malaria model (2.1) more easily, we work with fractional quantities instead of actual populations by scaling the population of each class by the total species population. We let:

$$e_h = \frac{E_h}{N_h}$$
 and $i_h = \frac{I_h}{N_h}$ and $r_h = \frac{R_h}{N_h}$ (2.4)

with

$$S_h = s_h N_h = (1 - e_h - i_h - r_h) N_h \tag{2.5}$$

and

$$e_v = \frac{E_v}{N_v}$$
 and $i_v = \frac{I_v}{N_v}$ (2.6)

with

$$S_v = s_v N_v = (1 - e_v - i_v) N_v. (2.7)$$

Differentiation of the scaling equations (2.4) and (2.6) gives us

$$\frac{dE_h}{dt} = \frac{de_h}{dt} N_h + e_h \frac{dN_h}{dt} \tag{2.8}$$

and

$$\frac{dE_v}{dt} = \frac{de_v}{dt}N_v + e_v \frac{dN_v}{dt} \tag{2.9}$$

and so on for the rest of the variables.

Solving for the derivatives of the scaled variables we obtain

$$\frac{de_h}{dt} = \frac{1}{N_h} \left[\frac{dE_h}{dt} - e_h \frac{dN_h}{dt} \right] \tag{2.10}$$

and

$$\frac{de_v}{dt} = \frac{1}{N_v} \left[\frac{dE_v}{dt} - e_v \frac{dN_v}{dt} \right] \tag{2.11}$$

and so on for the other variables.

This creates a new 7-dimensional system of equations with two dimensions for the two total population variables and five dimensions for the fractional population variables with disease:

$$\frac{de_h}{dt} = \sigma_{vh} \beta_{hv} \frac{N_v}{N_h} i_v \left(1 - e_h - i_h - r_h \right) - \left(\nu_h + \psi_h + \frac{\Lambda_h}{N_h} \right) e_h + \delta_h i_h e_h$$
(2.12a)

$$\frac{di_h}{dt} = \nu_h e_h - \left(\gamma_h + \delta_h + \psi_h + \frac{\Lambda_h}{N_h}\right) i_h + \delta_h i_h^2$$
 (2.12b)

$$\frac{dr_h}{dt} = \gamma_h i_h - \left(\rho_h + \psi_h + \frac{\Lambda_h}{N_h}\right) r_h + \delta_h i_h r_h \tag{2.12c}$$

$$\frac{dN_h}{dt} = \Lambda_h + \psi_h N_h - (\mu_{1h} + \mu_{2h} N_h) N_h - \delta_h i_h N_h$$
 (2.12d)

$$\frac{de_v}{dt} = \sigma_{vh} \left(\beta_{vh} i_h + \tilde{\beta}_{vh} r_h \right) (1 - e_v - i_v) - (\nu_v + \psi_v) e_v \qquad (2.12e)$$

$$\frac{di_v}{dt} = \nu_v e_v - \psi_v i_v \qquad (2.12f)$$

$$\frac{di_v}{dt} = \nu_v e_v - \psi_v i_v \tag{2.12f}$$

$$\frac{dN_v}{dt} = \psi_v N_v - (\mu_{1v} + \mu_{2v} N_v) N_v \tag{2.12g}$$

$$\frac{dN_v}{dt} = \psi_v N_v - (\mu_{1v} + \mu_{2v} N_v) N_v \tag{2.12g}$$

Note that e_v and i_v do not have any meaning when $N_v = 0$.

For this model (2.12), there exists a a domain where the system of equations is epidemiologically and mathematically well-posed. We define this domain, \mathcal{D} , as:

$$\mathcal{D} = \left\{ \begin{pmatrix} e_h \\ i_h \\ r_h \\ N_h \\ e_v \\ i_v \\ N_v \end{pmatrix} \in \mathbb{R}^7 \middle| \begin{array}{l} e_h \ge 0, \\ i_h \ge 0, \\ r_h \ge 0, \\ e_h + i_h + r_h \le 1, \\ N_h \ge M > 0, \\ e_v \ge 0, \\ i_v \ge 0, \\ e_v + i_v \le 1, \\ N_v \ge 0 \end{array} \right\}$$

$$(2.13)$$

for some positive M that depends on the parameter values. This domain, \mathcal{D} , is valid epidemiologically as the fractionally populations, e_h , i_h , r_h , e_v and i_v are all nonnegative and have sums over their species type that are less than or equal to 1. The human and mosquito populations, N_h and N_v , are positive and nonnegative, respectively. We require an artificial positive lower bound, M, on the human population because e'_h , i'_h and r'_h are not defined at $N_h = 0$.

Theorem 2.1 Assuming that the initial conditions lie in \mathcal{D} , the system of equations for the malaria model (2.12) has a unique solution that exists and remains in \mathcal{D} for all time $t \geq 0$.

Proof The right hand side of the system of equations (2.12) is continuous with continuous partial derivatives in \mathcal{D} . It remains to show that \mathcal{D} is forward-invariant. It is clear from (2.12) that if $e_h = 0$, then $e'_h \geq 0$; if $i_h = 0$, then $i'_h \geq 0$; if $e_v = 0$, then $e'_v \geq 0$; and if $e_v = 0$, then $e'_v \geq 0$. It is also true that if $e_h + i_h + r_h = 1$ then $e'_h + i'_h + r'_h < 1$; and if $e_v + i_v = 1$ then $e'_v + i'_v < 1$. Finally, we note that if $N_v = 0$, then $N'_v = 0$; and if $N_h = M$, then

$$N'_h = \Lambda_h + \psi_h M - \mu_{1h} M - \mu_{2h} M^2 - \delta_h i_h M$$

> $\Lambda_h + \psi_h M - \mu_{1h} M - \mu_{2h} M^2 - \delta_h M$.

Thus, $N'_h > 0$ for some M small enough, provided that $\Lambda_h > 0$. If $\Lambda_h = 0$, then we require $\psi_h > (\mu_{1h} + \delta_h)$ (with a different appropriate M small enough). However, in this paper, we will only consider the case with $\Lambda_h > 0$. Thus, none of the orbits can leave \mathcal{D} and a unique solution exists for all time.

3 Disease-Free Equilibrium Points and Reproductive Number

3.1 Existence of Disease-Free Equilibrium Points

We first look at equilibrium points where there is no disease. We define the "diseased" classes as the human or mosquito populations that are either exposed, infectious or recovered; that is, e_h , i_h , r_h , e_v and i_v .

Theorem 3.1 There are exactly two equilibrium points of the malaria model (2.12) on the intersection of \mathcal{D} and the boundary of the positive cone in \mathbb{R}^7 (which we denote by $\partial \mathbb{R}^7$). One equilibrium point contains only humans without disease (and no mosquitoes) and we label that as the mosquito-free equilibrium, x_{mfe} :

$$x_{mfe} = \left(0, 0, 0, \frac{(\psi_h - \mu_{1h}) + \sqrt{(\psi_h - \mu_{1h})^2 + 4\mu_{2h}\Lambda_h}}{2\mu_{2h}}, 0, 0, 0\right).$$
(3.1)

The second point contains humans and mosquitoes but no disease, which we label as the disease-free equilibrium, x_{dfe} :

$$x_{dfe} = \left(0, 0, 0, \frac{(\psi_h - \mu_{1h}) + \sqrt{(\psi_h - \mu_{1h})^2 + 4\mu_{2h}\Lambda_h}}{2\mu_{2h}}, 0, 0, \frac{\psi_v - \mu_{1v}}{\mu_{2v}}\right). \quad (3.2)$$

Proof We need to show that x_{mfe} and x_{dfe} are equilibrium points of (2.12); and that there are no other equilibrium points on $\mathcal{D} \cap \partial \mathbb{R}^7$. The first can be seen by substituting the equilibrium points, (3.1) and (3.2), into the system of equations (2.12).

We still need to show that there are no other equilibrium points on $\mathcal{D} \cap \partial \mathbb{R}^7$. Lemma A.1 states that on $\mathcal{D} \cap \partial \mathbb{R}^7$, $e_h = i_h = r_h = e_v = i_v = 0$. For $i_h = 0$, the only equilibrium point for N_h from (2.12d) is $N_h = ((\psi_h - \mu_{1h}) + \sqrt{(\psi_h - \mu_{1h})^2 + 4\mu_{2h}\Lambda_h})/(2\mu_{2h});$ and the only two equilibrium points for N_v from (2.12g) are $N_v = 0$ and $N_v = (\psi_v - \mu_{1v})/\mu_{2v}$. Thus, the only two equilibrium points on $\mathcal{D} \cap \partial \mathbb{R}^7$ are x_{mfe} and x_{dfe} .

For ease of notation, we label the positive equilibrium human and mosquito population values (in the absence of disease) by N_h^* and N_v^* , respectively.

$$N_h^* = \frac{(\psi_h - \mu_{1h}) + \sqrt{(\psi_h - \mu_{1h})^2 + 4\mu_{2h}\Lambda_h}}{2\mu_{2h}}$$

$$N_v^* = \frac{\psi_v - \mu_{1v}}{\mu_{2v}}$$
(3.3a)

$$N_v^* = \frac{\psi_v - \mu_{1v}}{\mu_{2v}} \tag{3.3b}$$

Reproductive Number 3.2

We use the next generation operator approach, as described by Diekmann etal. in [8] to define the reproductive number, R_0 , as the number of secondary infections that one infectious individual would create over the duration of the infectious period provided that everyone else is susceptible. We define the next generation operator, K, which provides the number of secondary infections in humans and mosquitoes caused by one generation of infectious humans and mosquitoes, as

$$K = \begin{pmatrix} 0 & K_{hv} \\ K_{vh} & 0 \end{pmatrix} \tag{3.4}$$

where

 K_{hv} : The number of humans that one mosquito infects through its infectious lifetime, assuming all humans are susceptible.

The number of mosquitoes that one human infects through the dura- K_{vh} : tion of the infectious period, assuming all mosquitoes are susceptible.

Using the ideas of Hyman and Li [12], we define K_{hv} and K_{vh} as a product of the probability of surviving till the infectious state, the number of contacts per unit time, the probability of transmission per contact and the duration of the infectious period:

$$K_{hv} = \frac{\nu_{v}}{\nu_{v} + \mu_{1v} + \mu_{2v}N_{v}^{*}} \cdot \sigma_{vh} \cdot \beta_{hv} \cdot \frac{1}{\mu_{1v} + \mu_{2v}N_{v}^{*}}$$
(3.5a)

$$K_{vh} = \frac{\nu_{h}}{\nu_{h} + \mu_{1h} + \mu_{2h}N_{h}^{*}} \cdot \frac{\sigma_{vh}N_{v}^{*}}{N_{h}^{*}} \cdot \beta_{vh} \cdot \frac{1}{\gamma_{h} + \delta_{h} + \mu_{1h} + \mu_{2h}N_{h}^{*}}$$
(3.5b)

$$+ \frac{\nu_{h}}{\nu_{h} + \mu_{1h} + \mu_{2h}N_{h}^{*}} \cdot \frac{\gamma_{h}}{\gamma_{h} + \delta_{h} + \mu_{1h} + \mu_{2h}N_{h}^{*}}$$
$$\cdot \frac{\sigma_{vh}N_{v}^{*}}{N_{h}^{*}} \cdot \tilde{\beta}_{vh} \cdot \frac{1}{\rho_{h} + \mu_{1h} + \mu_{2h}N_{h}^{*}} .$$

In (3.5a), $\nu_v/(\nu_v + \mu_{1v} + \mu_{2v}N_v^*)$ is the probability that a mosquito will survive

the exposed state to become infectious¹; σ_{vh} is the number of contacts that one mosquito has with humans per unit time; β_{hv} is the probability of transmission of infection from an infectious mosquito to a susceptible human; and $1/(\mu_{1v} +$ $\mu_{2v}N_v^*$) is the average duration of the infectious lifetime of the mosquito. In (3.5b), the total number of mosquitoes infected by one human is the sum of the new infections from the infectious and the recovered states. In the first term of K_{vh} , $\nu_h/(\nu_h + \mu_{1h} + \mu_{2h}N_h^*)$ is the probability that a human will survive the exposed state to become infectious; $\sigma_{vh}(N_v^*/N_h^*)$ is the number of contacts that one human has with mosquitoes per unit time; β_{vh} is the probability of transmission of infection from an infectious human to a susceptible mosquito; and $1/(\gamma_h + \delta_h + \mu_{1h} + \mu_{2h}N_h^*)$ is the average duration of the infectious period of a human. In the second term, $\nu_h/(\nu_h + \mu_{1h} + \mu_{2h}N_h^*)$ is the probability that a human will survive the exposed state to become infectious; $\gamma_h/(\gamma_h + \delta_h +$ $\mu_{1h} + \mu_{2h} N_h^*$ is the probability that the human will then survive the infectious state to move to the recovered state; $\sigma_{vh}(N_v^*/N_h^*)$ is the number of contacts that one human has with mosquitoes per unit time; β_{vh} is the probability of transmission of infection from a recovered human to a susceptible mosquito; and $1/(\rho_h + \mu_{1h} + \mu_{2h}N_h^*)$ is the average duration of the recovered period of a

We let R_0 be the spectral radius of the next generation operator, i.e.,

$$R_0^2 = K_{vh}K_{hv}.$$

Then, R_0^2 is the number of humans that one infectious human will infect, through a generation of infections in mosquitoes, assuming that previously all other humans and mosquitoes were susceptible.

Definition We define the reproductive number, R_0 , as

$$R_0 = \sqrt{K_{vh}K_{hv}} \tag{3.6}$$

where K_{vh} and K_{hv} are defined in (3.5).

3.3 Stability of Disease-Free Equilibrium Points

We conduct linear stability on the two equilibrium points without disease: (3.1) and (3.2). The Jacobian of the malaria model (2.12) has the form (3.7):

$$J = \begin{pmatrix} J_{11} & J_{12} & J_{13} & J_{14} & 0 & J_{16} & J_{17} \\ J_{21} & J_{22} & 0 & J_{24} & 0 & 0 & 0 \\ 0 & J_{32} & J_{33} & J_{34} & 0 & 0 & 0 \\ 0 & J_{42} & 0 & J_{44} & 0 & 0 & 0 \\ 0 & J_{52} & J_{53} & 0 & J_{55} & J_{56} & 0 \\ 0 & 0 & 0 & 0 & J_{65} & J_{66} & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & J_{77} \end{pmatrix}$$

$$(3.7)$$

¹In defining time periods and probabilities for R_0 , we use the original system of equations (2.1) and not the scaled equations (2.12). As the two models are equivalent, the reproductive number is the same with either definition: $\mu_{1h} + \mu_{2h}N_h^*$ is equivalent to $\psi_h + \Lambda_h/N_h^*$ and $\mu_{1v} + \mu_{2v}N_v^*$ is equivalent to ψ_v .

with

$$J_{11} = -\sigma_{vh}\beta_{hv}N_{v}i_{v}/N_{h} - (\nu_{h} + \psi_{h} + \Lambda_{h}/N_{h}) + \delta_{h}i_{h}$$

$$J_{12} = -\sigma_{vh}\beta_{hv}N_{v}i_{v}/N_{h} + \delta_{h}e_{h}$$

$$J_{13} = -\sigma_{vh}\beta_{hv}N_{v}i_{v}/N_{h}$$

$$J_{14} = -(\sigma_{vh}\beta_{hv}N_{v}i_{v}/N_{h}^{2})(1 - e_{h} - i_{h} - r_{h}) + \Lambda_{h}e_{h}/N_{h}^{2}$$

$$J_{16} = (\sigma_{vh}\beta_{hv}N_{v}/N_{h})(1 - e_{h} - i_{h} - r_{h})$$

$$J_{17} = (\sigma_{vh}\beta_{hv}i_{v}/N_{h})(1 - e_{h} - i_{h} - r_{h})$$

$$J_{21} = \nu_{h}$$

$$J_{22} = -(\gamma_{h} + \delta_{h} + \psi_{h} + \Lambda_{h}/N_{h}) + 2\delta_{h}i_{h}$$

$$J_{24} = \Lambda_{h}i_{h}/N_{h}^{2}$$

$$J_{33} = -(\rho_{h} + \psi_{h} + \Lambda_{h}/N_{h}) + \delta_{h}i_{h}$$

$$J_{44} = \Lambda_{h}r_{h}/N_{h}^{2}$$

$$J_{42} = -\delta_{h}N_{h}$$

$$J_{44} = \psi_{h} - \mu_{1h} - 2\mu_{2h}N_{h} - \delta_{h}i_{h}$$

$$J_{52} = \sigma_{vh}\beta_{vh}(1 - e_{v} - i_{v})$$

$$J_{53} = \sigma_{vh}\beta_{vh}(1 - e_{v} - i_{v})$$

$$J_{55} = -\sigma_{vh}(\beta_{vh}i_{h} + \tilde{\beta}_{vh}r_{h}) - (\nu_{v} + \psi_{v})$$

$$J_{56} = -\sigma_{vh}(\beta_{vh}i_{h} + \tilde{\beta}_{vh}r_{h})$$

$$J_{65} = \nu_{v}$$

$$J_{66} = -\psi_{v}$$

$$J_{77} = \psi_{v} - \mu_{1v} - 2\mu_{2v}N_{v}$$
(3.8u)

Theorem 3.2 The mosquito-free equilibrium point, x_{mfe} (3.1), is locally asymptotically stable if $\psi_v < \mu_{1v}$ and unstable if $\psi_v > \mu_{1v}$.

Proof The Jacobian evaluated at x_{mfe} (3.1) is a lower triangular matrix of the form

$$J = \begin{pmatrix} J_{11} & 0 & 0 & 0 & 0 & 0 & 0 \\ J_{21} & J_{22} & 0 & 0 & 0 & 0 & 0 \\ 0 & J_{32} & J_{33} & 0 & 0 & 0 & 0 \\ 0 & J_{42} & 0 & J_{44} & 0 & 0 & 0 \\ 0 & J_{52} & J_{53} & 0 & J_{55} & 0 & 0 \\ 0 & 0 & 0 & 0 & J_{65} & J_{66} & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & J_{77} \end{pmatrix} .$$
 (3.9)

The eigenvalues, simply the diagonal entries of the Jacobian, are:

$$\eta_1 = -(\nu_h + \psi_h + \Lambda_h/N_h^*)$$
(3.10a)

$$\eta_2 = -(\gamma_h + \delta_h + \psi_h + \Lambda_h/N_h^*) \tag{3.10b}$$

$$\eta_3 = -(\rho_h + \psi_h + \Lambda_h/N_h^*) \tag{3.10c}$$

$$\eta_4 = \psi_h - \mu_{1h} - 2\mu_{2h} N_h^* \tag{3.10d}$$

$$= -\sqrt{(\psi_h - \mu_{1h})^2 + 4\mu_{2h}\Lambda_h}$$

$$\eta_5 = -(\nu_v + \psi_v) \tag{3.10e}$$

$$\eta_6 = -\psi_v \tag{3.10f}$$

$$\eta_7 = \psi_v - \mu_{1v} \tag{3.10g}$$

We see that all eigenvalues are negative for $\psi_v < \mu_{1v}$ and one eigenvalue, η_7 , is positive for $\psi_v > \mu_{1v}$.

The mosquito free equilibrium point is thus locally asymptotically stable if the mosquito death rate is greater than the mosquito birth rate and unstable if the mosquito birth rate is greater than the mosquito death rate.

Theorem 3.3 The disease-free equilibrium point, x_{dfe} (3.2), is locally asymptotically stable if $R_0 < 1$ and $\psi_v > \mu_{1v}$; and is unstable if either $R_0 > 1$ or $\psi_v < \mu_{1v}$.

A full proof of this theorem can be found in Appendix A.1. It consists of evaluating the Jacobian, to find one eigenvalue that is always negative and one eigenvalue equal to $-(\psi_v - \mu_{1v})$, and using Descartes' Rule of Sign to show that all the remaining 5 eigenvalues are negative when $R_0 < 1$ and one of them is positive when $R_0 > 1$.

4 Endemic Equilibrium Points

Endemic equilibrium points are steady states where the disease persists in the population (all state variables are positive). The complexity of the system of equations (2.12) has prevented us from finding an explicit representation of the endemic equilibrium point(s). We use general bifurcation theorems to show the existence of at least 1 equilibrium point for all $R_0 > 1$. We are able to show that the transcritical bifurcation at $R_0 = 1$ is supercritical when $\delta_h = 0$ (there is no disease-induced death). However, numerical results show that the bifurcation can be subcritical for some positive values of δ_h , giving rise to endemic equilibria for $R_0 < 1$.

We first rewrite the equilibrium equations for (2.12) in the form of a nonlinear eigenvalue problem:

$$u = G(\zeta, u)$$

= $\zeta Lu + h(\zeta, u)$ (4.1)

where $u \in Y = \mathbb{R}^2$, a real Banach space with Euclidean norm, $\|\cdot\|$; $\zeta \in \mathbb{R}$ is the bifurcation parameter; L is a compact linear map on Y; and $h(\zeta, u)$ is $\mathcal{O}(\|u\|^2)$ uniformly on bounded ζ intervals. We take the equilibrium equations (the right hand side of (2.12)), reduce the dimension through some algebraic manipulations, and rewrite them in the form of (4.1) with

$$u = \left(\begin{array}{c} e_h \\ e_v \end{array}\right)$$

where e_h and e_v are equilibrium values. We use $\zeta = \sigma_{vh}$ for the bifurcation parameter. We also define $\Omega = \{\mathbb{R} \times Y\}$ so that the pair $(\zeta, u) \in \Omega$.

A theorem by Rabinowitz [22] (Thm 1.3) states that if ζ_0 is a characteristic value (reciprocal of an eigenvalue) of L of odd multiplicity, then there exists a nontrivial continuum of solution pairs, (ζ, u) of (4.1) that intersects the trivial solution (that is, $(\zeta, 0)$ for any ζ) at $(\zeta_0, 0)$ and continues to either infinity (is unbounded in Ω) or to $(\hat{\zeta}_0, 0)$ where $\hat{\zeta}_0$ is also a characteristic value of L of odd multiplicity.

We use this theorem to show that there exists a continuum of solution pairs $(\zeta, u) \in \Omega$ for the eigenvalue equation (4.1). To each of these solution-pairs, there corresponds an equilibrium-pair (ζ, x^*) of the malaria model (2.12), where ζ is a parameter value and $x^* \in \mathbb{R}^7$ is an equilibrium point of the malaria model (2.12). We define the equilibrium-pair, (ζ, x^*) , as the collection of a parameter value, ζ , and the corresponding equilibrium point, x^* , for that parameter value.

Theorem 4.1 Assuming that the mosquito birth rate is greater than the mosquito death rate $(\psi_v > \mu_{1v})$, the malaria model (2.12) has a continuum of equilibriumpairs, (ζ, x^*) , that connects the point (ξ_1, x_{dfe}) to infinity (specifically is unbounded for $\zeta \in \mathbb{R}$ but is bounded for $x^* \in \mathbb{R}^7$) in the positive cone of \mathbb{R}^7 . The number $\xi_1 = 1/\sqrt{AB}$ where A and B are defined in the Appendix (A.25).

We give a proof of this theorem in Appendix A.2.

Theorem 4.2 Assume $\psi_v > \mu_{1v}$. The bifurcation point at $\zeta = \xi_1$ corresponds to $R_0 = 1$. For the set of ζ for which there exists an equilibrium-pair (ζ, x^*) , the corresponding set of values for R_0 includes, but is not necessarily equal to, $(1, \infty)$. Thus, there exists at least 1 endemic equilibrium point of the malaria model (2.12) for all $R_0 > 1$.

Proof As $\zeta = \sigma_{vh}$, some algebraic manipulations of R_0 (3.6) produces

$$R_0 = \zeta \sqrt{AB}. (4.2)$$

Thus, R_0 is linearly related to ζ ; and when $\zeta = \xi_1$, $R_0 = 1$. As the continuum of equilibrium-pairs connects (ξ_1, x_{dfe}) to infinity and is bounded in \mathbb{R}^7 , it exists for all $\zeta > \xi_1$, and thus an endemic equilibrium exists for all $R_0 > 1$. Note that it is possible, though not necessary, for the continuum of equilibrium-pairs to include values of $\zeta < \xi_1$ ($R_0 < 1$).

Typically in epidemiological models, bifurcations at $R_0 = 1$ tend to be supercritical (i.e., positive endemic equilibria exist for $R_0 > 1$ near the bifurcation point). It turns out that in this model, (2.12), a supercritical (forward) bifurcation does not necessarily occur at $R_0 = 1$. We can show, however, that in the absence of disease induced death ($\delta_h = 0$), the bifurcation is supercritical (forward).

We determine the direction of the bifurcation using the Lyapunov-Schmidt method as described by Cushing (1998) [7]. We begin by expanding the terms of the nonlinear eigenvalue equation (4.1) about the bifurcation point, $(\xi_1, 0)$. The expanded variables are

$$u = 0 + \varepsilon u^{(1)} + \varepsilon^2 u^{(2)} + \dots$$
 (4.3a)

$$\zeta = \xi_1 + \varepsilon \zeta_1 + \varepsilon^2 \zeta_2 + \dots \tag{4.3b}$$

$$L = L \tag{4.3c}$$

$$h(\zeta, u) = h(\xi_1 + \varepsilon \zeta_1 + \varepsilon^2 \zeta_2 + \dots, \varepsilon u^{(1)} + \varepsilon^2 u^{(2)} + \dots)$$

$$= \varepsilon^2 h_2(\xi_1, u^{(1)}) + \dots$$
(4.3d)

We substitute the expansions (4.3) into the eigenvalue equation (4.1) and evaluate at different orders of ε .

Theorem 4.3 Assuming $\psi_v > \mu_{1v}$, in the absence of disease-induced death $(\delta_h = 0)$, the bifurcation at $R_0 = 1$ is supercritical (forward).

The proof involves substitutions of the expansions (4.3) into the eigenvalue equation (4.1) up to second order in ε and an application of the Fredholm Alternative. Details of this proof are in Appendix A.3.

For positive values of δ_h , it is possible for this model to exhibit a subcritical bifurcation (sometimes called a "backward" bifurcation) in which case, near the bifurcation point, positive endemic equilibria exist for $R_0 < 1$. Other examples of epidemiological models with subcritical (backward) bifurcations at $R_0 = 1$ include those described by Castillo-Chavez and Song [6], Gómez-Acevedo and Yi [11] and van den Driessche and Watmough [24].

Although we cannot prove the existence of a subcritical (backward) bifurcation, we show through numerical examples that it is possible for some positive values of δ_h . This is important because it implies that there can be a stable endemic equilibrium even if R_0 is less than 1.

We first use the bifurcation software program AUTO [10] to create bifurcation diagrams around $R_0=1$. We show two examples of these bifurcation diagrams in Figure 4.1. One has all parameter values as described in Table 4.1 except for the bifurcation parameter, σ_{vh} , which is varied as shown in the figure. The other curve has parameter values described in Table 4.1, except for $\delta_h=3.41938\times 10^{-5}$ and the bifurcation parameter, σ_{vh} , which is also varied as shown in the figure.

For the curve with $\delta_h = 3.45392 \times 10^{-4}$, we can see both unstable and stable endemic equilibrium points. There is a subcritical (backward) bifurcation at $\sigma_{vh} = 0.5779$ ($R_0 = 1$); and a saddle-node bifurcation at $\sigma_{vh} = 0.5515$

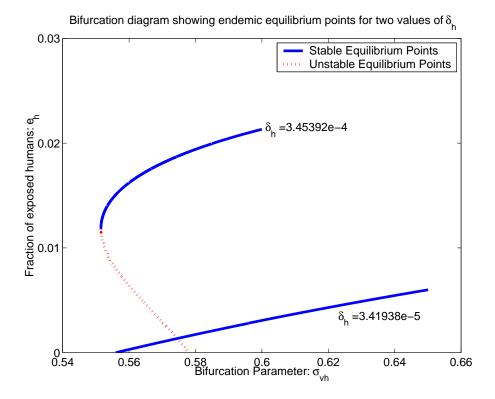


Figure 4.1: Two bifurcation diagrams for (2.12) showing only the endemic equilibrium points. The top curve (labeled $\delta_h = 3.45392 \times 10^{-4}$) is for parameter values described in Table 4.1. The bottom curve (labeled $\delta_h = 3.41938 \times 10^{-5}$) has the same parameters as the first curve, except for δ_h . Only the equilibrium value of the fraction of exposed humans, e_h , is shown on the y-axis. The bifurcations are explained in more detail in the text.

 $(R_0 = 0.9543)$. Thus a locally asymptotically stable endemic equilibrium is possible for values of R_0 below 1. Though we do not show the plots here, further bifurcation analysis has shown that even as σ_{vh} is increased to large levels, the size of the projection of the endemic equilibrium on the fractional infected groups increases monotonically, and the equilibrium point remains stable.

For comparison we show the bifurcation diagram with $\delta_h = 3.41938 \times 10^{-5}$. Here, we only see a stable branch of endemic equilibrium points. There is a supercritical (forward) bifurcation at $\sigma_{vh} = 0.5559$ ($R_0 = 1$). There are no endemic equilibrium points for R_0 less than 1. Though we do not show the plots here, further bifurcation analysis has shown, for these parameter values, that even as σ_{vh} is increased to large levels, the size of the projection of the endemic equilibrium on the fractional infected groups increases monotonically, and the equilibrium point remains stable.

Table 4.1: The values of parameters for which there exist positive endemic equilibrium points when $R_0 < 1$: $R_0 = 0.9690$. The unit of time is days.

$$\begin{array}{lll} \Lambda_h = 3.285 \times 10^{-2} \\ \psi_h = 7.666 \times 10^{-5} & \psi_v = 0.4000 \\ \beta_{vh} = 0.8333 & \beta_{hv} = 2.000 \times 10^{-2} \\ \tilde{\beta}_{vh} = 8.333 \times 10^{-3} & \\ \sigma_{vh} = 0.5600 & \\ \nu_h = 8.333 \times 10^{-2} & \nu_v = 0.1000 \\ \gamma_h = 3.704 \times 10^{-3} & \\ \delta_h = 3.45392 \times 10^{-4} & \\ \rho_h = 1.460 \times 10^{-2} & \\ \mu_{1h} = 4.212 \times 10^{-5} & \mu_{1v} = 0.1429 \\ \mu_{2h} = 1.000 \times 10^{-7} & \mu_{2v} = 2.279 \times 10^{-4} \end{array}$$

We now focus on an example with parameter values described in Table 4.1. The reproductive number corresponding to these parameter values is $R_0=0.9690$. Most of these parameter values are within the bounds of a realistically feasible range, with the exception of the mosquito birth rate which has been significantly increased to lower the value of the reproductive number below 1. The value of δ_h corresponds to a death rate of 12.62% of infected humans per year. We numerically² find four equilibrium points: two on the boundary of, and two in, the positive cone of \mathbb{R}^7 . The two equilibrium points on the boundary are the mosquito-free equilibrium point, x_{mfe} , $N_h=771.3$. and the disease-free equilibrium point, x_{dfe} . The two equilibrium points inside the positive cone are two endemic equilibrium points. Linear stability analysis shows that the "larger" endemic equilibrium point is locally asymptotically stable, while the "smaller" point is unstable. Further linear analysis with an increased value of $\sigma_{vh}=0.6$ and all other parameters as in Table 4.1 (with $R_0=1.038$) shows that there is one stable endemic equilibrium point.

Figure 4.2 shows simulations of the original unscaled equations (2.1) for parameter values in Table 4.1. These plots illustrate the stability of the "larger" endemic equilibrium in the presence of a stable disease-free equilibrium point.

5 Summary and Conclusions

In this paper, we analyzed a 7-dimensional ODE model for the transmission of malaria, with 4 variables for humans and 3 variables for mosquitoes. We showed that there exists a domain where the model is epidemiologically and mathematically well-posed.

For this model, we were able to show the existence of two equilibrium points with no disease: one with only humans and no mosquitoes, x_{mfe} , and one with

 $^{^2{\}rm The}$ numerical solutions to the equilibrium equations were found using the ${\tt NSolve}$ command in Mathematica.

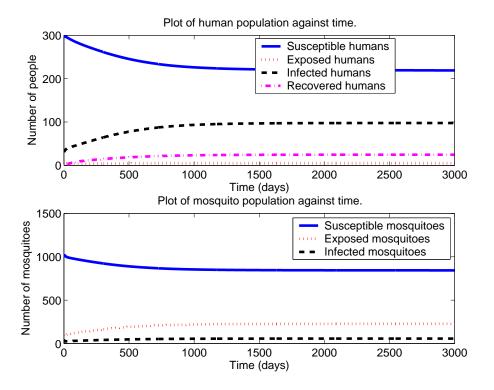


Figure 4.2: A numerical simulation of the malaria model (2.1) (using the original system variables before normalization) with parameter values defined in Table 4.1. These parameters correspond to $R_0=0.969$. The initial conditions used were $S_h=300$, $E_h=10$, $I_h=30$, $R_h=0$, $S_v=1000$, $E_v=100$ and $I_v=50$; which correspond to $e_h=0.0294$, $i_h=0.0882$, $r_h=0$, $N_h=340$, $e_v=0.0870$, $i_v=0.0435$ and $N_v=1150$. The system approaches an endemic equilibrium point. We thus have a stable endemic equilibrium for $R_0<1$. The simulations were conducted using MATLAB's ode45 — a variable order Runge-Kutta method — with a relative tolerance of 10^{-5} and an absolute tolerance of 10^{-7} .

both humans and mosquitoes, x_{dfe} . The equilibrium point with no mosquitoes, x_{mfe} , is locally asymptotically stable if the mosquito birth rate, ψ_v , is lesser than the mosquito death rate, μ_{1v} .

We defined a reproductive number, R_0 that is epidemiologically accurate in that it provides the expected number of new infections (in mosquitoes or humans) from one infectious individual (human or mosquito) over the duration of the infectious period given that all other members of the population are susceptible. We showed that, provided the mosquito birth rate is greater than the mosquito death rate, if $R_0 < 1$, then the disease-free equilibrium point, x_{dfe} ,

is locally asymptotically stable and if $R_0 > 1$, then x_{dfe} is unstable.

We also proved that an endemic equilibrium point exists for all $R_0 > 1$ with a transcritical bifurcation at $R_0 = 1$. The analysis and the numerical simulations showed that for $\delta_h = 0$, and for some small positive values of δ_h , there is a supercritical (forward) transcritical bifurcation at $R_0 = 1$ with an exchange of stability between the disease-free equilibrium and the endemic equilibrium as shown in Figure 5.1(a). For larger values of δ_h , there is a subcritical (backward) transcritical bifurcation at $R_0 = 1$, with an exchange of stability between the endemic equilibrium and the disease free equilibrium; and there is a saddle-node bifurcation at $R_0 = R_0^*$ for some $R_0^* < 1$. A schematic of this bifurcation diagram is shown in Figure 5.1(b).

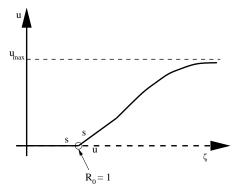
While we do not have any analytical results on the stability of the endemic equilibrium for large values of R_0 , the numerical results suggest that the equilibrium is stable. However, it follows from Theorem 2.1 that all orbits of the system of equations (2.12) are bounded. Thus, if the endemic equilibrium were to lose stability, then there would exist a nonequilibrium attractor (such as a limit cycle or strange attractor), though for this model we have no evidence for nonequilibrium attractors.

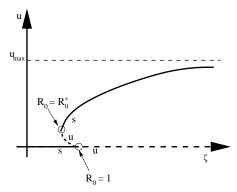
The possible existence of a subcritical (backward) bifurcation at $R_0 = 1$ and a saddle-node bifurcation at some $R_0^* < 1$, as shown in Figure 5.1(b), can have strong implications for public health. Simply reducing R_0 to a value below 1 is not always sufficient to eradicate the disease; it is now necessary to reduce R_0 to a value less than R_0^* to ensure that there is no endemic equilibrium. The existence of a saddle-node bifurcation also implies that in some areas with endemic malaria, it may be possible to significantly reduce prevalence or eradicate the disease with small increases in control programs (a small reduction in R_0 so that it is less than R_0^*). Note that it may also be possible in some areas where malaria has been eradicated, for a slight disruption, like a change in environmental or control variables or an influx of infectious humans or mosquitoes, for the disease to reestablish itself in the population with a significant increase in the prevalence rate (increasing R_0 above R_0^* or moving the system into the basin of attraction of the endemic equilibrium).

The possibility of a subcritical (backward) bifurcation in our model is also a significant difference from the model of Ngwa and Shu [21], as that model only exhibited a supercritical (forward) bifurcation at $R_0 = 1$.

In future papers, we plan to conduct several studies of the model presented here. These studies will include a sensitivity analysis on the reproductive number and the endemic equilibrium. As we have an explicit expression for R_0 , we can analytically evaluate its sensitivity to the different parameter values. We also wish to numerically evaluate the sensitivity of the endemic equilibrium to the parameter values. This will allow us to compare different control strategies in various parts of the world for efficiency and effectiveness in reducing malaria mortality and morbidity.

We also plan to study the effects of the environment on the spread of malaria. Mosquito populations depend heavily on environmental factors such as rainfall, temperature and humidity. These factors typically vary periodically. We want





(a) A supercritical bifurcation for small values of δ_h . We have proved the stability of the disease-free equilibrium point (locally asymptotically stable for $R_0 < 1$ and unstable for $R_0 > 1$) and the existence of the endemic equilibrium point for all $R_0 > 1$. We have also proved that the bifurcation is supercritical when $\delta_h = 0$. Numerical simulations suggest that the endemic equilibrium is stable for $R_0 > 1$. Numerical results also suggest that for some small positive values of δ_h , the bifurcation is supercritical. We have no analytical results for the stability of the endemic equilibrium as R_0 approaches ∞ .

(b) A subcritical bifurcation for large values of δ_h . We have proved the stability of the disease-free equilibrium point (locally asymptotically stable for $R_0 < 1$ and unstable for $R_0 > 1$) and the existence of the endemic equilibrium point for all $R_0 > 1$. Numerical simulations show that for some values of δ_h , when $R_0 < 1$, there exist two endemic equilibrium points, the smaller of which is unstable while the larger is locally asymptotically stable. For the same δ_h , as ζ (σ_{vh}) is decreased, the two endemic equilibrium points disappear; and as ζ is increased to a corresponding value of R_0 greater than 1, there is only one stable endemic equilibrium. The results show a subcritical bifurcation at $R_0 = 1$ and a saddle-node bifurcation at $R_0 = R_0^*$ for some $R_0^* < 1$ (dependent on the parameter values). We have no analytical results for the stability of the endemic equilibrium as R_0 approaches ∞ .

Figure 5.1: Schematics of the two possible bifurcation scenarios for different values of δ_h for the constant parameter malaria model (2.12). It is important to note that this figure is a cartoon, which summarizes the results for the bifurcation, and not an actual numerical study of the bifurcation.

to incorporate these effects by analyzing the original malaria model with selected periodic coefficients, such as the mosquito birth rate. We would like to explore this periodically forced model for features not seen in the autonomous model, including appropriate adaptions to the definition of the reproductive number and the endemic states. This should provide a more accurate picture of the malaria epidemics than that obtained from models using parameter values that are averaged over the seasons.

An ultimate goal is to validate this model by applying it to particular areas in the world infected with malaria. We will compare predicted endemic states obtained from the model using estimated parameter values from a given location

to the actual prevalence data in that location.

A Lemmas and Proofs of Theorems

Lemma A.1 For all equilibrium points on $\mathcal{D} \cap \partial \mathbb{R}^7$, $e_h = i_h = r_h = e_v = i_v = 0$.

Proof We need to show that for an equilibrium point in \mathcal{D} , if any one of diseased classes is zero, all the rest are also equal to zero. For ease of notation, we write the statements below.

```
\begin{array}{lll} (\mathrm{H1}): \ e_h = 0. \\ (\mathrm{H2}): \ i_h = 0. \\ (\mathrm{H3}): \ r_h = 0. \\ (\mathrm{H4}): \ e_v = 0. \\ (\mathrm{H5}): \ i_v = 0. \\ (\mathrm{H6}): \ (\mathrm{H1}) \ \mathrm{and} \ (\mathrm{H2}) \ \mathrm{and} \ (\mathrm{H3}). \\ (\mathrm{H7}): \ (\mathrm{H4}) \ \mathrm{and} \ (\mathrm{H5}). \end{array}
```

We show by setting the right hand side of (2.12) equal to 0, that if any one of the above statements is true, all the others are true. For $i'_h = 0$, (H1) is true if and only if (H2) is true³. Similarly, for $r'_h = 0$, (H2) is true if and only if (H3) is true. Thus, if any one of (H1), (H2) or (H3) is true, (H6) is true. From $e'_h = 0$, we see that if (H6) is true, then (H5) is true. Also, for $i'_v = 0$, (H4) is true if and only if (H5) is true. Thus, if either one of (H4) or (H5) is true, then (H7) is true. Finally, for $e'_v = 0$, if (H7) is true, then both (H2) and (H3) are true.

A.1 Proof of Theorem 3.3

Proof of Theorem 3.3 The Jacobian evaluated at x_{dfe} (3.2) is of the form:

$$J = \begin{pmatrix} J_{11} & 0 & 0 & 0 & 0 & J_{16} & 0 \\ J_{21} & J_{22} & 0 & 0 & 0 & 0 & 0 \\ 0 & J_{32} & J_{33} & 0 & 0 & 0 & 0 \\ 0 & J_{42} & 0 & J_{44} & 0 & 0 & 0 \\ 0 & J_{52} & J_{53} & 0 & J_{55} & 0 & 0 \\ 0 & 0 & 0 & 0 & J_{65} & J_{66} & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & J_{77} \end{pmatrix}.$$
(A.1)

As the fourth and seventh columns (corresponding to the total human and mosquito populations) contain only the diagonal terms, these diagonal terms

³ As the right-hand side of (2.12b) is a quadratic function of i_h , there are 2 possible solutions of i_h when $i'_h = 0$ and $e_h = 0$. However, the nonzero solution of i_h is greater than 1 and thus outside of \mathcal{D} .

form two eigenvalues of the Jacobian:

$$\eta_6 = \psi_h - \mu_{1h} - 2\mu_{2h} N_h^*$$
(A.2a)

$$= -\sqrt{(\psi_h - \mu_{1h})^2 + 4\mu_{2h}\Lambda_h}$$

$$\eta_7 = \psi_v - \mu_{1v} - 2\mu_{2v} N_v^*
= -(\psi_v - \mu_{1v}).$$
(A.2b)

The other 5 eigenvalues are the roots of the characteristic equation of the matrix formed by excluding the $4^{\rm th}$ and $7^{\rm th}$ rows and columns of the Jacobian (A.1):

$$A_5\eta^5 + A_4\eta^4 + A_3\eta^3 + A_2\eta^2 + A_1\eta + A_0 = 0 (A.3)$$

with

$$A_5 = 1 \tag{A.4a}$$

$$A_4 = B_1 + B_2 + B_3 + B_4 + B_5 \tag{A.4b}$$

$$A_3 = B_1B_2 + B_1B_3 + B_1B_4 + B_1B_5 + B_2B_3 + B_2B_4 + B_2B_5$$
(A.4c)
+ $B_3B_4 + B_3B_5 + B_4B_5$

$$A_2 = B_1B_2B_3 + B_1B_2B_4 + B_1B_2B_5 + B_1B_3B_4 + B_1B_3B_5 + (A.4d)$$

$$B_1B_4B_5 + B_2B_3B_4 + B_2B_3B_5 + B_2B_4B_5 + B_3B_4B_5$$

$$A_1 = B_1 B_2 B_3 B_4 + B_1 B_2 B_3 B_5 + B_1 B_2 B_4 B_5 + B_1 B_3 B_4 B_5 + (A.4e)$$

$$B_2 B_3 B_4 B_5 - B_6 B_7 B_8 B_9$$

$$A_0 = B_1 B_2 B_3 B_4 B_5 - (B_3 B_6 B_7 B_8 B_9 + B_6 B_7 B_9 B_{10} B_{11}) \tag{A.4f}$$

and

$$B_{1} = \nu_{h} + \psi_{h} + \Lambda_{h}/N_{h}^{*}$$

$$= \nu_{h} + \frac{1}{2} \left((\psi_{h} + \mu_{1h}) + \sqrt{(\psi_{h} - \mu_{1h})^{2} + 4\mu_{2h}\Lambda_{h}} \right)$$
(A.5a)

$$B_2 = \gamma_h + \delta_h + \psi_h + \Lambda_h / N_h^* \tag{A.5b}$$

$$= \gamma_h + \delta_h + \frac{1}{2} \left((\psi_h + \mu_{1h}) + \sqrt{(\psi_h - \mu_{1h})^2 + 4\mu_{2h}\Lambda_h} \right)$$

$$B_3 = \rho_h + \psi_h + \Lambda_h / N_h^* \tag{A.5c}$$

$$= \rho_h + \frac{1}{2} \left((\psi_h + \mu_{1h}) + \sqrt{(\psi_h - \mu_{1h})^2 + 4\mu_{2h}\Lambda_h} \right)$$

$$B_4 = \nu_v + \psi_v \tag{A.5d}$$

$$B_5 = \psi_v \tag{A.5e}$$

$$B_6 = \sigma_{vh} \beta_{hv} N_v^* / N_h^* \tag{A.5f}$$

$$B_7 = \nu_h \tag{A.5g}$$

$$B_8 = \sigma_{vh} \beta_{vh} \tag{A.5h}$$

$$B_9 = \nu_v \tag{A.5i}$$

$$B_{10} = \gamma_h \tag{A.5j}$$

$$B_{11} = \sigma_{vh}\tilde{\beta}_{vh}. \tag{A.5k}$$

In a similar manner to [21], we show the stability of the disease-free equilibrium changes as R_0 passes through 1 by using Descartes' Rule of Sign. Korn and Korn [16] in §1.6-6(c) state Descartes' Rule of Sign as: the number of positive real roots of a real algebraic equation (A.6)

$$a_n x^n + a_{n-1} x^{n-1} + \ldots + a_1 x + a_0 = 0$$
 (A.6)

is equal to the number, N_a , of sign changes in the sequence, $a_n, a_{n-1}, \ldots, a_0$, of coefficients, where the vanishing terms are disregarded, or it is less than N_a by a positive even integer. We show that when $R_0 < 1$, all the coefficients of the characteristic equation (A.3) are positive, so all the eigenvalues of the Jacobian (A.1) have negative real part. We then show that when $R_0 > 1$, there is one sign change in the sequence A_5, A_4, \ldots, A_0 , so there is one eigenvalue with positive real part and the disease free equilibrium point is unstable.

As all the B_i are positive, A_5 , A_4 , A_3 and A_2 are all positive. We will now show that when $R_0 < 1$, both A_1 and A_0 are positive. We will then show that when $R_0 > 1$, A_0 is negative. Thus, when $R_0 < 1$, all the coefficients of the characteristic equation (A.3) are positive, and when $R_0 > 1$, there is only one change in sign when the coefficients are arranged as in Descartes' Rule of Sign.

When R_0 is less (greater) than 1, R_0^2 is also less (greater) than 1 since R_0 is strictly positive. The expression for R_0^2 (3.6) can be written, in terms of B_i , as

$$R_0^2 = \frac{B_3 B_6 B_7 B_8 B_9 + B_6 B_7 B_9 B_{10} B_{11}}{B_1 B_2 B_3 B_4 B_5}. (A.7)$$

Thus for $R_0 < 1$,

$$\frac{B_3 B_6 B_7 B_8 B_9}{B_1 B_2 B_3 B_4 B_5} < 1$$

so

$$B_6B_7B_8B_9 < B_1B_2B_4B_5$$

and as all other terms in A_1 are positive, $A_1 > 0$. $R_0 < 1$ also implies that

$$B_3B_6B_7B_8B_9 + B_6B_7B_9B_{10}B_{11} < B_1B_2B_3B_4B_5$$

and thus $A_0 > 0$.

Similarly, when $R_0 > 1$

$$B_3B_6B_7B_8B_9 + B_6B_7B_9B_{10}B_{11} > B_1B_2B_3B_4B_5$$

and $A_0 < 0$. Note that the Jacobian of the disease-free equilibrium (3.2) has one eigenvalue equal to 0 at $R_0 = 1$.

Thus, we can say that the disease free-equilibrium point, x_{dfe} , is locally asymptotically stable if $R_0 < 1$ (the disease will not spread) and $\psi_v > \mu_{1h}$ (the mosquitoes will not become extinct); and unstable if $R_0 > 1$, or if $\psi_v < \mu_{1h}$. \square

A.2 Proof of Theorem 4.1

Proof of Theorem 4.1 The equilibrium equations for (2.12) are shown below in (A.8). For the remainder of this section, §4 and Appendix A.2, we will use the terms, e_h , i_h , r_h , N_h , e_v , i_v and N_v to represent their respective equilibrium values and not their actual values at a given time, t.

$$\sigma_{vh}\beta_{hv}\frac{N_{v}}{N_{h}}i_{v}(1-e_{h}-i_{h}-r_{h})-$$

$$(\nu_{h}+\psi_{h}+\Lambda_{h}/N_{h})e_{h}+\delta_{h}i_{h}e_{h}=0 \qquad (A.8a)$$

$$\nu_{h}e_{h}-(\gamma_{h}+\delta_{h}+\psi_{h}+\Lambda_{h}/N_{h})i_{h}+\delta_{h}i_{h}^{2}=0 \qquad (A.8b)$$

$$\gamma_{h}i_{h}-(\rho_{h}+\psi_{h}+\Lambda_{h}/N_{h})r_{h}+\delta_{h}i_{h}r_{h}=0 \qquad (A.8c)$$

$$\Lambda_{h}+\psi_{h}N_{h}-(\mu_{1h}+\mu_{2h}N_{h})N_{h}-\delta_{h}i_{h}N_{h}=0 \qquad (A.8d)$$

$$\sigma_{vh}\left(\beta_{vh}i_{h}+\tilde{\beta}_{vh}r_{h}\right)(1-e_{v}-i_{v})-(\nu_{v}+\psi_{v})e_{v}=0 \qquad (A.8e)$$

$$\nu_{v}e_{v}-(\psi_{v})i_{v}=0 \qquad (A.8f)$$

$$\psi_{v}N_{v}-(\mu_{1v}+\mu_{2v}N_{v})N_{v}=0 \qquad (A.8g)$$

We do not attempt to rewrite the entire system (A.8) in the form of (4.1), but reduce the equilibrium equations to a two-dimensional system for e_h and e_v .⁴ We do so by solving for the other variables, either explicitly as functions of the parameters, or in terms of e_h and e_v .

We solve (A.8g) for N_v , explicitly expressing the positive equilibrium for the total mosquito population in terms of parameters (exactly as in the disease-free case (3.3b)).

$$N_v = \frac{\psi_v - \mu_{1v}}{\mu_{2v}} \tag{A.9}$$

Solving for i_v in (A.8f) in terms of e_v we find:

$$i_v = \frac{\nu_v}{\psi_v} e_v. \tag{A.10}$$

Similarly, we write the positive equilibrium for the total human population, N_h , in terms of i_h from (A.8d) as

$$N_h = \frac{(\psi_h - \mu_{1h} - \delta_h i_h) + \sqrt{(\psi_h - \mu_{1h} - \delta_h i_h)^2 + 4\mu_{2h}\Lambda_h}}{2\mu_{2h}}.$$
 (A.11)

Using (A.11) in (A.8c), we solve for r_h in terms of i_h .

$$r_h = \frac{2\gamma_h i_h}{2\rho_h + (\psi_h + \mu_{1h} - \delta_h i_h) + \sqrt{(\psi_h - \mu_{1h} - \delta_h i_h)^2 + 4\mu_{2h}\Lambda_h}}$$
(A.12)

Given the nonlinear nature of (A.8b), it is not feasible (or useful) to solve for i_h in terms of e_h explicitly. We therefore use (A.11) to rewrite (A.8b) as

$$f(e_h, i_h) = 0 (A.13)$$

⁴This also better serves our purposes as the theorem by Rabinowitz requires a bifurcation from the zero equilibrium point; and N_h and N_v have positive equilibrium values.

where

$$f(e_h, i_h) = \nu_h e_h -$$

$$\left[\gamma_h + \delta_h + \frac{1}{2} \left((\psi_h + \mu_{1h} - \delta_h i_h) + \sqrt{(\psi_h - \mu_{1h} - \delta_h i_h)^2 + 4\mu_{2h} \Lambda_h} \right) \right] i_h$$
(A.14)

and use the Implicit Function Theorem (Korn and Korn [16], §4.5-7) to approximate (A.13) by a Taylor polynomial for i_h as a function of e_h . The partial derivatives of $f(e_h, i_h)$ are

$$\frac{\partial f}{\partial e_h}(e_h, i_h) = \nu_h \tag{A.15}$$

$$\frac{\partial f}{\partial i_h}(e_h, i_h) = \frac{1}{2} \delta_h \left[i_h + \frac{\psi_h - \mu_{1h} - \delta_h i_h}{\sqrt{(\psi_h - \mu_{1h} - \delta_h i_h)^2 + 4\Lambda_h \mu_{2h}}} \right] i_h \tag{A.16}$$

$$-\left[\gamma_h + \delta_h + \frac{1}{2}\left((\psi_h + \mu_{1h} - \delta_h i_h) + \sqrt{(\psi_h - \mu_{1h} - \delta_h i_h)^2 + 4\mu_{2h}\Lambda_h}\right)\right]$$

As $f(e_h, i_h)$ and its partial derivatives with respect to e_h and i_h exist, and are continuous in a neighbourhood of (0,0); and $\frac{\partial f}{\partial i_h}$ is nonzero at $i_h=0$; there exists a unique differentiable function

$$i_h = y(e_h)$$

around $i_h = 0$ and $e_h = 0$ that is equivalent to (A.13). We approximate this function with a Taylor polynomial of the form

$$i_h = y_1 e_h + y_2 e_h^2 + \dots$$
 (A.17)

where

$$y_1 = -\frac{\frac{\partial f}{\partial e_h}}{\frac{\partial f}{\partial i_h}}\bigg|_{i_h = e_h = 0}$$

and

$$y_2 = -\frac{1}{\left(\frac{\partial f}{\partial i_h}\right)^3} \times$$

$$\left[\left(\frac{\partial^2 f}{\partial e_h^2} \right) \left(\frac{\partial f}{\partial i_h} \right)^2 - 2 \left(\frac{\partial^2 f}{\partial e_h \partial i_h} \right) \left(\frac{\partial f}{\partial e_h} \right) \left(\frac{\partial f}{\partial i_h} \right) + \left(\frac{\partial^2 f}{\partial i_h^2} \right) \left(\frac{\partial f}{\partial e_h} \right)^2 \right] \bigg|_{i_h = e_h = 0}.$$

An evaluation of these expressions provides:

$$y_1 = \frac{\nu_h}{\gamma_h + \delta_h + \frac{1}{2} \left((\psi_h + \mu_{1h}) + \sqrt{(\psi_h - \mu_{1h})^2 + 4\mu_{2h}\Lambda_h} \right)}$$
(A.18)

and

$$y_{2} = \frac{1}{\sqrt{(\psi_{h} - \mu_{1h})^{2} + 4\mu_{2h}\Lambda_{h}}} \times (A.19)$$

$$\frac{\delta_{h}\nu_{h}^{2}(\psi_{h} - \mu_{1h})}{\left[\gamma_{h} + \delta_{h} + \frac{1}{2}\left((\psi_{h} + \mu_{1h}) + \sqrt{(\psi_{h} - \mu_{1h})^{2} + 4\mu_{2h}\Lambda_{h}}\right)\right]^{3}}.$$

Finally, we substitute the Taylor approximation for i_h (A.17) into r_h (A.12) and N_h (A.11), and then all three, along with i_v (A.10) and N_v (A.9) into the equilibrium equations for e_h (A.8a) and e_v (A.8e), to provide second order approximations to the equilibrium equations

$$0 = f_{1,10}e_h + f_{1,01}e_v + f_{1,11}e_he_v + f_{1,20}e_h^2 + f_{1,02}e_v^2 + \mathcal{O}(u^3)(A.20a)$$

$$0 = f_{2,10}e_h + f_{2,01}e_v + f_{2,11}e_he_v + f_{2,20}e_h^2 + f_{2,02}e_v^2 + \mathcal{O}(u^3)(A.20b)$$

where

$$u = \begin{pmatrix} e_h \\ e_v \end{pmatrix} \tag{A.21}$$

and

$$f_{1-10} = -\left[\nu_h + \frac{1}{2}\left((\psi_h + \mu_{1h}) + \sqrt{(\psi_h - \mu_{1h})^2 + 4\mu_{2h}\Lambda_h}\right)\right]$$
 (A.22a)

$$f_{1.01} = \sigma_{vh} \frac{2\mu_{2h}\nu_v\beta_{hv}(\psi_v - \mu_{1v})}{\psi_v\mu_{2v}\left((\psi_h - \mu_{1h}) + \sqrt{(\psi_h - \mu_{1h})^2 + 4\mu_{2h}\Lambda_h}\right)}$$
(A.22b)

$$f_{1.01} = \sigma_{vh} \frac{2\mu_{2h}\nu_{v}\beta_{hv}(\psi_{v} - \mu_{1v})}{\psi_{v}\mu_{2v}\left((\psi_{h} - \mu_{1h}) + \sqrt{(\psi_{h} - \mu_{1h})^{2} + 4\mu_{2h}\Lambda_{h}}\right)}$$
(A.22b)

$$f_{2.10} = \sigma_{vh} \frac{\nu_{h}}{\gamma_{h} + \delta_{h} + \frac{1}{2}\left((\psi_{h} + \mu_{1h}) + \sqrt{(\psi_{h} - \mu_{1h})^{2} + 4\mu_{2h}\Lambda_{h}}\right)}$$
(A.22c)

$$\times \left[\beta_{vh} + \frac{\gamma_{h}\tilde{\beta}_{vh}}{\rho_{h} + \frac{1}{2}\left((\psi_{h} + \mu_{1h}) + \sqrt{(\psi_{h} - \mu_{1h})^{2} + 4\mu_{2h}\Lambda_{h}}\right)}\right]$$

$$f_{2,01} = -(\psi_v + \nu_v). \tag{A.22d}$$

Although we have expressions for the coefficients of the second order terms, we do not explicitly show them here as they are lengthy and not needed for our

To apply Theorem 1.3 of Rabinowitz [22], we factor out $\zeta = \sigma_{vh}$, after some algebraic manipulations on (A.20), to produce

$$\begin{pmatrix} e_h \\ e_v \end{pmatrix} = \zeta \begin{pmatrix} 0 & A \\ B & 0 \end{pmatrix} \begin{pmatrix} e_h \\ e_v \end{pmatrix} + \mathcal{O} \begin{pmatrix} \begin{pmatrix} e_h \\ e_v \end{pmatrix} \end{pmatrix}^2 \tag{A.23}$$

or

$$u = \zeta L u + h(\zeta, u) \tag{A.24}$$

where

$$L = \left(\begin{array}{cc} 0 & A \\ B & 0 \end{array}\right)$$

with

$$A = \frac{1}{\nu_{h} + \frac{1}{2} \left((\psi_{h} + \mu_{1h}) + \sqrt{(\psi_{h} - \mu_{1h})^{2} + 4\mu_{2h}\Lambda_{h}} \right)} \times$$

$$\frac{2\mu_{2h}\nu_{v}\beta_{hv}(\psi_{v} - \mu_{1v})}{\psi_{v}\mu_{2v} \left((\psi_{h} - \mu_{1h}) + \sqrt{(\psi_{h} - \mu_{1h})^{2} + 4\mu_{2h}\Lambda_{h}} \right)}$$

$$B = \left(\beta_{vh} + \frac{\gamma_{h}\tilde{\beta}_{vh}}{\rho_{h} + \frac{1}{2} \left((\psi_{h} + \mu_{1h}) + \sqrt{(\psi_{h} - \mu_{1h})^{2} + 4\mu_{2h}\Lambda_{h}} \right)} \right) \times (A.25b)$$

$$\frac{\nu_{h}}{(\psi_{v} + \nu_{v}) \left(\gamma_{h} + \delta_{h} + \frac{1}{2} \left((\psi_{h} + \mu_{1h}) + \sqrt{(\psi_{h} - \mu_{1h})^{2} + 4\mu_{2h}\Lambda_{h}} \right) \right)}.$$

The matrix, L, has 2 distinct eigenvalues: $\pm \sqrt{AB}$. Characteristic values of a matrix are the reciprocals of its eigenvalues. For the matrix, L, we denote the two characteristic values by $\xi_1 = 1/\sqrt{AB}$ and $\xi_2 = -1/\sqrt{AB}$. The right eigenvector corresponding to the characteristic value, ξ_1 is

$$v = \begin{pmatrix} \sqrt{A} \\ \sqrt{B} \end{pmatrix}. \tag{A.26}$$

We note here that B is always positive and A is positive if and only if $\psi_v > \mu_{1v}$. Thus ξ_1 is real and corresponds to the dominant eigenvalue of L if and only if $\psi_v > \mu_{1v}$. We require this condition for the existence of the endemic equilibrium because otherwise the mosquito death rate would be greater than the mosquito birth rate so the positive equilibrium for the total mosquito population would be unstable; and the mosquito population would asymptotically approach zero.

By Theorem 1.3 of Rabinowitz [22], we know that there is a continuum of solution pairs $(\zeta, u) \in \Omega$, whose closure contains the point $(\xi_1, 0)$, that either meets ∞ (is unbounded) or the point $(\xi_2, 0)$. We denote the continuum of solution pairs emanating from $(\xi_1, 0)$ by \mathscr{C}_1 where $\mathscr{C}_1 \subset \Omega$; and from $(\xi_2, 0)$ by \mathscr{C}_2 where $\mathscr{C}_2 \subset \Omega$. We introduce the sets

$$Z_1 = \{ \zeta \in \mathbb{R} | \exists u \text{ such that } (\zeta, u) \in \mathscr{C}_1 \}$$
 (A.27a)

$$U_1 = \{ u \in Y \mid \exists \zeta \text{ such that } (\zeta, u) \in \mathscr{C}_1 \}$$
 (A.27b)

$$Z_2 = \{ \zeta \in \mathbb{R} | \exists u \text{ such that } (\zeta, u) \in \mathscr{C}_2 \}$$
 (A.27c)

$$U_2 = \{ u \in Y \mid \exists \zeta \text{ such that } (\zeta, u) \in \mathscr{C}_2 \}.$$
 (A.27d)

We denote the positive cone in Y, $\{(e_h, e_v)|e_h > 0 \text{ and } e_v > 0\}$, by Y^+ ; and the boundary of Y^+ by ∂Y^+ .

As shown in Lemma A.4, the initial direction of U_i , the projection of the continuum of solution pairs \mathscr{C}_i in Y, near the bifurcation point $(\xi_i,0)$, is given by the eigenvector corresponding to the characteristic value, ξ_i — where i is either 1 or 2. Additionally, from Lemma A.1, there are no equilibrium points on ∂Y^+ other than $e_h = e_v = 0$, so $U_1 \cap \partial Y^+ = (0,0)$ and $U_2 \cap \partial Y^+ = (0,0)$; and hence

 U_1 and U_2 cannot pass through ∂Y^+ . The eigenvector, v (A.26), corresponding to ξ_1 contains only positive terms, while the eigenvector corresponding to ξ_2 is $(-\sqrt{A} \quad \sqrt{B})^{\mathrm{T}}$; thus U_1 enters and cannot leave Y^+ while U_2 is always outside Y^+ . As U_1 and U_2 cannot meet, \mathscr{C}_1 and \mathscr{C}_2 do not intersect and by the Theorem of Rabinowitz, \mathscr{C}_1 meets ∞ (is unbounded).

By Lemma A.2, the set U_1 is bounded for all finite positive ζ , so \mathscr{C}_1 only meets ∞ at $\zeta = \infty$. By Lemma A.3, for every $u \in U_1$, there corresponds at least one x^* in the positive cone of \mathbb{R}^7 , except for u = (0,0) which corresponds to x_{dfe} (on the boundary of the positive cone of \mathbb{R}^7). Thus, there exists a continuum of equilibrium-pairs $(\zeta, x^*) \in {\mathbb{R} \times \mathbb{R}^7}$ that connects the point (ξ_1, x_{dfe}) to ∞ in such a way that the ζ component is unbounded.

Lemma A.2 The set, U_1 , is bounded for all finite ζ .

Proof It suffices to show that the e_h and e_v values of the ω -limit set of the solutions of (2.12) are bounded above by 1. As e_h and e_v are positive (because U_1 is in Y^+), by Lemma A.3, all other state variables are also positive. Thus we see from (2.12a) that if $e_h > 1$, then $e'_h < 0$; and similarly from (2.12e) we see that if if $e_v > 1$, then $e'_v < 0$. Thus the endemic equilibrium point(s) is contained in a bounded region for all finite ζ .

Lemma A.3 The point $u = (0,0) \in Y$ corresponds to $x_{dfe} \in \mathbb{R}^7$ (on the boundary of the positive cone of \mathbb{R}^7). For every other solution pair $(\zeta, u) \in \mathcal{C}_1$, there corresponds at least one equilibrium pair $(\zeta, x^*) \in \{\mathbb{R} \times \mathbb{R}^7\}$ where x^* is in the positive cone of \mathbb{R}^7 .

Proof We first show that u = (0,0) corresponds to x_{dfe} . As $e_h = e_v = 0$, by Theorem 3.1 we know that the only 2 possible equilibrium points are x_{mfe} and x_{dfe} . As we picked the positive mosquito equilibrium population in solving for N_v (A.9), the equilibrium point that we bifurcate from is x_{dfe} .

We now show that for every $\zeta \in Z_1$ there exists at least one x^* in the positive cone of \mathbb{R}^7 for the corresponding $u \in U_1$. For this, we need to show that for every positive and bounded e_h and e_v , there exist positive and bounded i_h , r_h , i_v , N_h and N_v . By looking at the equilibrium equation for i_v (A.10), we see that for every positive and bounded e_v there exists a positive and bounded i_v . The equilibrium equation for N_v has a positive and bounded solution depending only on parameter values (A.9). The equilibrium equation for i_h (A.13) may be written as

$$e_{h} = \frac{\gamma_{h} + \delta_{h} + \frac{1}{2} \left((\psi_{h} + \mu_{1h} - \delta_{h} i_{h}) + \sqrt{(\psi_{h} - \mu_{1h} - \delta_{h} i_{h})^{2} + 4\mu_{2h} \Lambda_{h}} \right)}{\nu_{h}} i_{h}.$$
(A.28)

The right-hand side of (A.28) is a continuous function of i_h with range $[0, \infty)$ so for every positive and bounded e_h , there exists at least one positive and bounded i_h . The equilibrium equations for r_h (A.12) and N_h (A.11) show that for every positive and bounded i_h there exists a positive and bounded r_h and N_h , respectively.

A.3 Proof of Theorem 4.3

Evaluating the substitution of the expansions (4.3) into the eigenvalue equation (A.24) at $\mathcal{O}(\varepsilon^0)$ produces 0 = 0 which gives us no information. We need to calculate the $\mathcal{O}(\varepsilon^1)$ terms.

Lemma A.4 The initial direction of the branch of equilibrium points, $u^{(1)}$ near the bifurcation point $(\xi_1, 0)$, is equal to the eigenvector of L corresponding to the characteristic value, ξ_1 .

Proof Evaluating the substitution of the expansions (4.3) into the eigenvalue equation (A.24) at $\mathcal{O}(\varepsilon^1)$ we obtain:

$$u^{(1)} = \xi_1 L u^{(1)}.$$

This implies that $u^{(1)}$ is the eigenvector of L corresponding to the eigenvalue $1/\xi_1$, v (A.26). Thus, close to the bifurcation point, the equilibrium point can be approximated by $e_h = \varepsilon \sqrt{A}$ and $e_v = \varepsilon \sqrt{B}$.

Lemma A.5 The bifurcation at $\zeta = \xi_1$ of the nonlinear eigenvalue equation (A.24) is supercritical if $\zeta_1 > 0$ and subcritical if $\zeta_1 < 0$ where

$$\zeta_1 = -\frac{w \cdot h_2}{w \cdot Lv} \tag{A.29}$$

where v is the right eigenvector of L and w is the left eigenvector of L corresponding to the eigenvalue $1/\xi_1$.

Proof Evaluating the substitution of the expansions (4.3) into the eigenvalue equation (A.24) at $\mathcal{O}(\varepsilon^2)$ we obtain:

$$u^{(2)} = \xi_1 L u^{(2)} + \zeta_1 L u^{(1)} + h_2$$

which we can rewrite as

$$(\mathbb{I} - \xi_1 L)u^{(2)} = \zeta_1 L v + h_2 \tag{A.30}$$

where \mathbb{I} is the 2×2 identity matrix. As ξ_1 is a characteristic value of L, $(\mathbb{I}-\xi_1 L)$ is a singular matrix. Thus, for (A.30) to have a solution, $\zeta_1 L v + h_2$ must be in the range of $(\mathbb{I}-\xi_1 L)$, ie. it must be orthogonal to the null space of the adjoint of $(\mathbb{I}-\xi_1 L)$. The null space of the adjoint of $(\mathbb{I}-\xi_1 L)$ is spanned by the left eigenvector of L (corresponding to the eigenvalue $1/\xi_1$), which we denote by $w:=\begin{pmatrix} \sqrt{B} & \sqrt{A} \end{pmatrix}$. The Fredholm condition for the solvability of (A.30) gives us

$$w \cdot (\zeta_1 L v + h_2) = 0.$$

This requires

$$\zeta_1 = -\frac{w \cdot h_2}{w \cdot Lv}.$$

If ζ_1 is positive, then for small positive ε , u>0 and $\zeta>\xi_1$ and we have a supercritical (forward) bifurcation. Similarly, if ζ_1 is negative, then for small positive ε , u>0 and $\zeta<\xi_1$ and we have a subcritical (backward) bifurcation.

Proof of Theorem 4.3 When $\delta_h = 0$, we can explicitly evaluate $h(\zeta, u)$ in the nonlinear eigenvalue equation (A.24) from the equilibrium equations (A.20) as

$$h = \zeta \begin{pmatrix} C_{(\delta_h = 0)} e_h e_v \\ D_{(\delta_h = 0)} e_h e_v \end{pmatrix}$$
 (A.31)

since the coefficients of all the other higher order terms are zero. We have explicit representations for $C_{(\delta_h=0)}$ and $D_{(\delta_h=0)}$, but we do show them here. It suffices to say that both $C_{(\delta_h=0)}$ and $D_{(\delta_h=0)}$ are negative. From (A.31) and (4.3) we can evaluate the second order expansion, h_2 .

$$h_{2} = \xi_{1} \begin{pmatrix} C_{(\delta_{h}=0)} \sqrt{A} \sqrt{B} \\ D_{(\delta_{h}=0)} \sqrt{A} \sqrt{B} \end{pmatrix}$$

$$= \begin{pmatrix} C_{(\delta_{h}=0)} \\ D_{(\delta_{h}=0)} \end{pmatrix}$$
(A.32)

As h_2 contains only negative terms and w, v and L contain only nonnegative terms, (A.29) implies that ζ_1 is positive. Thus, by Lemma A.5, with no disease-induced death, for any positive values of the other parameters there is a supercritical (forward) bifurcation at $R_0 = 1$.

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